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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/312,351 05/14/99 WOLFF J MIRUS.006

HM12/0920

MARK K JOHNSON
PO BOX 510644
NEW BERLIN WI 53131-0644

EXAMINER

SCHNIZER, R

ART UNIT

PAPER NUMBER

1632

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DATE MAILED: 09/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action SummaryApplication No.
09/312,351

Applicant(s)

Wolff

Examiner

Richard Schnlzer

Group Art Unit

1632☐ Responsive to communication(s) filed on _____☐ This action is **FINAL**.☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim☒ Claim(s) 1-18 is/are pending in the applicatOf the above, claim(s) 1-6 and 15-17 is/are withdrawn from consideration☐ Claim(s) _____ is/are allowed.☒ Claim(s) 7-14 and 18 is/are rejected.☐ Claim(s) _____ is/are objected to.☐ Claims _____ are subject to restriction or election requirement.**Application Papers**☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.☐ The drawing(s) filed on _____ is/are objected to by the Examiner.☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.☐ The specification is objected to by the Examiner.☐ The oath or declaration is objected to by the Examiner.**Priority under 35 U.S.C. § 119**☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been☐ received.☐ received in Application No. (Series Code/Serial Number) _____☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).**Attachment(s)**☒ Notice of References Cited, PTO-892☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2☐ Interview Summary, PTO-413☐ Notice of Draftsperson's Patent Drawing Review, PTO-948☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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DETAILED ACTION

Applicant's election of group I, claims 7-14 and 18 in Paper No. 5 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-6 and 15-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 5.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is indefinite because it is unclear how a compound can comprise a compound. It appears that applicant intends to claim a composition comprising two compounds which are not

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covalently linked. If the two compounds are covalently linked, then they comprise a single compound.

Claim 18 is indefinite because it recites a disulfide molecule without antecedent basis. Claim 18 is dependent on claim 12 which recites disulfide bonds which are part of a molecule, however no disulfide molecule is recited. Claim 18 will be examined as if it were drawn to a disulfide-containing molecule.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-14 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al (Proc. Nat. Acad. Sci. USA 87(9): 3410-3414, 5/1990), as evidenced by MacGillivray et al (Proc. Nat. Acad. Sci. USA 79(8): 2504-2508, 4/1982).

Wagner teaches compositions for the delivery of DNA into cells. The compositions comprise human transferrin, which is a polyamphipathic compound, covalently linked to a polycation. The polycation is complexed to polyanionic DNA, and the entire complex is used to transfect cultured cells. Human transferrin comprises at least 19 disulfides (see for example MacGillivray, abstract), and the polylysine moiety is attached to transferrin by disulfide linkage.

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The instant specification teaches that cystines are cleaved more rapidly than oxidized glutathione, and that their component thiols, when reduced, have a lower pKa than glutathione. See page 2 lines 27-32. Transferrin is a ligand and a bifunctional molecule as it binds to both iron, and a cellular receptor. The composition of Wagner is also bifunctional in that it delivers both iron and DNA. Finally it is noted that cultured cells are considered to be microorganisms, thus Wagner satisfies the limitation of claim 12, part b.

Thus Wagner anticipates the claims.

MacGillivray is not relied upon for this rejection, but is merely cited to illustrate the inherent properties of transferrin.

Claims 7-14 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Stassen et al (Thrombosis and Haemostasis 74(2): 646-654, 8/1995), as evidenced by Elliott et al (J. Pharm. Exp. Therapeut. 273(1): 280-284, 4/1995) and Voet (In Biochemistry, Second Edition, John Wiley and Sons, Publishers, 1995).

Stassen teaches a compound comprising bovine pancreatic trypsin inhibitor (BPTI, aprotinin) and the neutral polymer, polyethylene glycol. The compound was administered to hamsters. BPTI is a polypeptide which can be considered a polyamphipathic compound because it comprises both charged and nonpolar moieties, yet it is also known in the art as a polycation (see Elliott, abstract). BPTI comprises three disulfide bonds, which are formed as a result of a series of intramolecular disulfide interchange reactions. See Voet, pages 196-198, especially

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Fig. 8-7, enclosed. This appears to meet the limitations of claim 7 part (c) and claim 12, part (iii), which require activation of a disulfide by intramolecular attack. Further, the instant specification teaches that cystines are cleaved more rapidly than oxidized glutathione, and that their component thiols, when reduced, have a lower pKa than glutathione. See page 2 lines 27-32. BPTI can be considered a ligand of trypsin, and can be considered bifunctional in that it can be used to inhibit trypsin and a variety of other proteases including factor Xa, factor VIIa-tissue factor complex, factor XIa, and plasma kallikrein.

Thus Stassen anticipates the claims.

Elliott and Voet are not relied upon for this rejection, but are merely cited to illustrate the inherent properties of BPTI.

Claim Rejections - 35 USC § 103

Claims 7-14 and 18 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Wagner et al (Proc. Nat. Acad. Sci. USA 87(9): 3410-3414, 5/1990), as evidenced by Lodish et al (J. Biol. Chem 266(23): 14835-14838, 8/1991).

The teachings of Wagner are summarized in the preceding rejection, however the issue of activation of disulfides by intramolecular attack was not considered.

Human transferrin comprises at least 19 disulfide bonds. Lodish showed that if folding of human transferrin is interrupted by cyclosporin A *in vivo*, a single species of transferrin is formed

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which comprises an intermediate pattern of disulfide bonding distinct from that of the mature species of transferrin. Conversion of the intermediate form of transferrin into the mature form requires breakage of existing disulfides and establishment of new, permanent ones. Thus it seems more likely than not that at least some of these reactions occur through intramolecular attack by free cysteine residues.

Thus Wagner anticipates the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached on Mondays and Thursdays between the hours of 6:20 AM and 3:50 PM, and on Tuesdays, Wednesdays and Fridays between the hours of 7:00 AM and 4:30 PM (Eastern time). The examiner is off every other Friday, but is usually in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at 703-305-6608. The FAX phone numbers for art unit 1632 are 703-308-4242 and 703-305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is 703-308-0196.

Richard Schnizer, Ph. D.

Scott D. Pribe
SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER